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FURTHER STUDIES ON THE TRANSFORMATIONS OF UNSATURATED ALDEHYDES BY FERMENTING BAKER'S YEAST: A FACILE SYNTHESIS OF L-OLIVOMYCOSE

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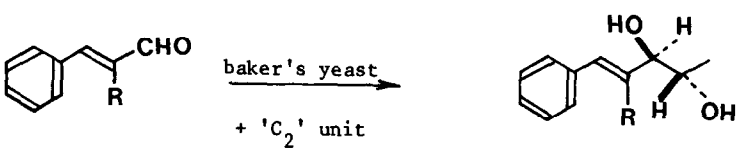
A current trend in natural products chemistry is the search of chiral reagents for asymmetric synthesis,[1] and considerable attention is being focused [2] on biologically mediated transformations of non conventional substrates as potential sources of optically active starting materials.

Among the several biological systems explored up to now [2], baker's yeast seems of particular interest because of the variety of the reactions it performs [3] and because it is commercially available, thus overcoming the problem of growing cultures and making it an attractive shelf reagent. We have already reported [4] obtaining, from C_6-C_3 α,β-unsaturated aldehydes and fermenting baker's yeast, C_6-C_5, optically active erythro methyl diols, and their use as starting materials in the synthesis of the optically active forms of deoxy- and methyl-branched deoxy sugars [5] and of D(-)-allomuscarine [6]. The above diols are expected to arise upon reduction of the α-ketols formed by acyloin type condensation from the aldehydes and a C_2 unit, as indicated in the following equation,



R = H, CH_3, Br

and seemed of interest to explore further the substrate specificity of this type of transformation and the synthetic potential of the product obtained.

Thus, the aldehydes (1) and (2), incubated with fermenting baker's yeast (commercial brand: Distillerie Italiane) under the conditions in which cinnamaldehyde and α-methylcinnamaldehyde give the diols (6) and (7),[4] afforded unreacted starting materials and the corresponding alcohols ($-CH_2OH$ instead of -CHO in (1) and (2)). Even the presence of added acetaldehyde, which greatly increases the yields of (6) and (7) from the corresponding C_6-C_3 aldehydes, did not lead to the formation of the expected diols from (1) and (2).

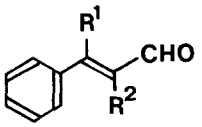
(E)-β-methylcinnamaldehyde (3) afforded without CH_3CHO ca. 10% of oily (8)§, $[\alpha]_D$ -6,7°¶, whereas 3-methyl-5-phenyl-penta-2,4-dien-1-al (4), shown by ^1H-n.m.r. studies to be a 1:1 mixture of the 2Z and 2E isomers, gave rise to the diol (9), in ca. 10% yield, showing $[\alpha]_D$ -7,6°, together with an approximately 6:4 mixture (by g.l.c.) of the 2Z and 2E alcohols, respectively ((4), with CH_2OH replacing -CHO). Similarly, the 2E aldehyde (5) gave in 15% yield the crystalline diol (10), m.p. 120°C, $[\alpha]_D$ +7,6°.

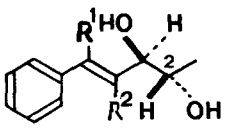
In so far as general conclusions can be drawn from the above experiments, the present results indicate that the reaction(s) involved in the overall conversion indicated in the reaction equation exhibits some requirements regarding the type of substituent in the α-position and the geometry of the α-double bond.

The synthetic potential of the products thus obtained is demonstrated by the conversion of (10) into the optically active form of the methyl-branched deoxy sugar L-olivomycose (2,6-dideoxy-3-C-methyl-L-arabino-hexose) (15), which also provides a configurational assignement for compound (10).

¶ if not otherwise stated, optical rotations were taken in $CHCl_3$, c= 1, at 20°C

§ the stereochemistry depicted in (8) and (9) is conjectural for positions 2 and 3





(1) R^1= H; R^2= CH_2CH_3

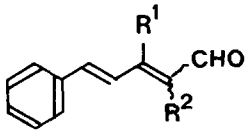
(2) R^1=H; R^2= $CH_2CH_2CH_3$

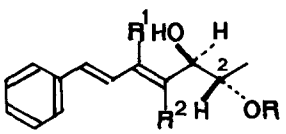
(3) R^1= CH_3; R^2= H

(6) R^1 =R^2= H

(7) R^1= H; R^2= CH_3

(8) R^1= CH_3; R^2= H





(4) R^1= CH_3; R^2= H

(5) R^1= H; R^2= CH_3

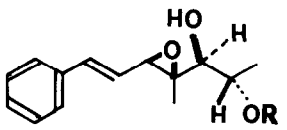
(9) R^1= CH_3; R^2= R^3= H

(10) R^1= R^3= H; R^2= CH_3

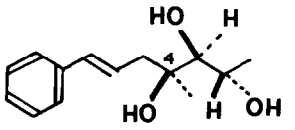
(11) R^1= H; R^2= Me; R^3= COC_6H_5

Thus, treatment of compound (10) with 1 mol. eq. of benzoyl chloride in CH_2Cl_2-pyridine gave the monobenzoate (11), as shown by the shift of the H-2 signal from 3,95 δ to 5,30 δ, $[\alpha]_D$ -9,7°. This compound when reacted in benzene with 1 mol. eq. of 3-chloroperoxybenzoic acid gave an unstable oily epoxide (12), readily converted with $LiAlH_4$ in Et_2O, at -10°C, into the triol (13), showing signal in the ^{1}H-n.m.r. spectrum due to the methyl group in position 4 at 1.20 δ. Compound (13) was converted into L-olivomycose (15) by ozonolysis

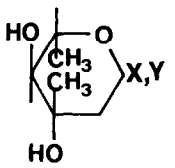
of the double bond of (13), followed by oxidative work up to the lactone (14), which was then reduced by known procedures [7] to L-olivomycose (15), m.p. 107-109°C, $[\alpha]_D$ -21° (c, 1 in water, 24 h); these physical constant are in agreement with



(12) R= COC_6H_5

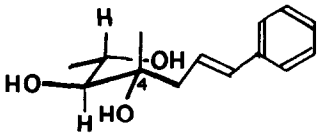


(13)



(14) X,Y= O

(15) X,Y= H,OH



literature values [8]. The reaction sequence allows the assignement of 2S,3R for the absolute configuration of compound (10). This is in agreement with the previous results in related series [5].

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